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09/702,283	10/30/2000	Benjamin Oshlack	200.1116US	1434

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EXAMINER
CELSA, BENNETT M

ART UNIT	PAPER NUMBER
1639	7

DATE MAILED: 09/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

file copy

Office Action Summary

Application No.	Applicant(s)
09/702,283	Oshlack et al.
Examiner	**Art Unit**
Bennett Celsa	1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jul 9, 2003* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-3 and 5-38* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-3 and 5-38* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

Applicant's amendment dated 7/9/03 in paper no. 8 is acknowledged.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of the Claims

Claims 1-3 and 5-38 are currently pending and under consideration.

Election/Restriction

2. Applicant's election with traverse of capsules as an oral dosage formulation and hydrocodone with the additives (e.g. Eudragit RS/RL as the "controlled release material" and stearyl alcohol) of Example 3, which applicant asserts reads on claims 1-3 and 5-41 in Paper No. 6 is again acknowledged. The election of species was made final in the prior office action.

Withdrawn Objection (s) and/or Rejection (s)

Applicant's amendment (e.g. inserting a trademarked product in the claims) has overcome the indefinite rejection of claims 16-18, 20, 27, 33 and 34 in the prior office action. However, applicant's amendment has a necessitated a new ground of rejection below.

Outstanding Objection(s) and/or Rejection (s)

3. Claims 1-3 and 5-38 are rejected under 35 U.S.C. 102(a,b,e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Oshlack et al. US Pat. No. 5,639,476 (6/97).

The presently claimed invention is directed to: controlled release oral dosage forms (e.g. tablets, capsule) comprising:

hydrocodone (or pharmaceutical salts) AND

"controlled release material to render said dosage form suitable for twice-a-day administration to a human patient ... said dosage form providing a therapeutic effect for at least 12 hours". Preferred suitable "controlled release materials" include ammonio-methacrylate copolymers of acrylic/methacrylic acid esters having low content of quaternary ammonium groups (e.g. Eudragit RS and/or /RL as the "controlled release material" as disclosed in elected Example 3). The hydrocodone may be dispersed in a (multiparticulate) matrix in which the multiparticles are disposed in a pharmaceutically acceptable capsule (e.g. see claims 2, 3 and 5).

The presently claimed compositions result in *various pharmacologic parameters* including:

a. " C12/Cmax ratio of 0.55 to 0.85" (E.g. claims 1, 36, 37);

b. "Plasma concentration of hydrocodone of at least 8 ngm/ml at from about 2 to about 8 hours after administration ... a dosage form containing 15mg hydrocloride bitartrate" (E.g. See dependent claims 14-15);

c. " *mean* C12/Cmax ratio of 0.55 to 0.85" (E.g. claim 38);

d. "rate of absorption during the time period from Tmax to about 12 hours after oral administration ... from about 55% to about 85% of the rate of elimination during the same time period" (E.g. claim 31);

e. "providing a Tmax of hydrocodone in-vivo at from about 2 to about 8 hours" and "providing a C12/Cmax ratio of 0.55 to 0.85" (E.g. see claim 32: see also Tmax values in dependent claims 11-13). See also dependent claims 27-30 for more Tmax parameters;

f. "after a first administration providing a Cmax of hydrocodone which is less than about 50% of the Cmax of an equivalent dose of an immediate release hydrocodone reference formulation" (E.g. see claim 33; dependent claims 16-17);

g. "after a first administration providing a time to 80% mean Cmax which is about 90% to about 110% of the time to 80% mean Cmax of an equivalent dose of an immediate release hydrocodone reference formulation" (E.g. see claim 34; dependent claim18); or "80% mean Cmax of hydrocodone from about .5 to about 1.5 hours (e.g. see dependent claim 19: see also dependent claims 21-26 for variations thereof; "a 90% mean Cmax which is about 150% to about 250% of the time to 90% Cmax of an equivalent dose of immediate release hydrocodone reference formulation" (e.g. see dependent claim 20); "a 90% mean Cmax of hydrocodone from about 1.5 to about 2.5 hours" (and variations thereof: see e.g. dependent claims 21--22)

h. "Tmax of about 2 mg/hr to about 4 mg/hr", "a mean in-vivo absorption rate from Tmax to about 12 hours after administration which is from about 0.08 mg/hr to about 0.4 mg/hr" ... "based

on oral administration of a dosage form containing 15mg hydrocodone bitartrate". (E.g. see claim 35);

I. "An in vitro release of at least 18% to about 42.5% by weight of the hydrocodone or salt from the dosage form at one hour ... " (E.g. see claim 7);

j. "Dissolution rate in vitro" (determined by USP Paddle/Basket method at 100 rmp in 900 ml aqueous buffer at a pH of 1.2 or 7.5 at 37 degrees celsius) of:

from about 25 to about 65% ... after 2hrs;

from about 45 to about 85% ... after 4hrs; and

greater than about 60% ... after 8 hrs (See E.g. dependent claims 7-10), respectively).

The Oshlack et al. Patent reference teaches controlled release oral dosage forms (e.g. tablets, capsule) comprising:

OPIOID analgesics (or pharmaceutical salts: e.g. see patent claims 1 and 6) AND

"controlled release material to render said dosage form suitable for twice-a-day administration to a human patient e.g. "said dosage form providing a therapeutic effect for at least 12 hours" (e.g. see patent claim 3). Oshlac et al. teach "controlled release materials" within the scope of the presently claimed invention which include ammonio-methacrylate copolymers of acrylic/methacrylic acid esters having low content of quaternary ammonium groups. E.g. patent claim 1; col. 4-5; 7-12 with Eudragit RS and/or /RL as the "controlled release material" being most preferred (e.g. see col. 9 ; and patent examples). . The opioid analgesic may be dispersed in a (multiparticulate) matrix in which the multiparticles are disposed in a pharmaceutically

acceptable capsule (e.g. examples; patent claim 4). The Oshlack et al. Teaching of opioid analgesics as the most preferred active agent (e.g. see examples and patent claims) with the preferred opioid analgesics comprising less than 15 members, one of which is hydrocodone (e.g. see paten claim 6) would render the selection of hydrocodone by one of ordinary skill in the art immediately envisaged (e.g. anticipates), or alteratively obvious; thus arriving at compositions containing ingredients within the scope of the presently claimed invention. E.g. see See *In re Schaumann*, 572 F.2d 312. 197 USPQ 5 (CCPA 1978); MPEP 2131.02. The Oshlack et al. reference compositions further discloses controlled release profiles (e.g. see col 4, particularly lines 40-60; col. 11-12; alterable by changing resin concentrations see col. 10 and 13); and methods of manufacture (e.g. of multiparticles: col. 13-16) which are clearly within the scope of the presently claimed invention (e.g. compare with present specification).

Accordingly, the Oshlack et al. reference anticipates or alternatively renders obvious compositions (and methods of making and use) within the scope of the presently claimed invention; in which the resulting compositions MUST *inherently* possess *the various pharmacologic parameters (e.g. a. to j. Above)* as presently claimed. The patent office lacks the necessary facilities to make comparisons between prior art and presently claimed compositions.

Discussion

Applicant's amendment and arguments directed to the above prior art rejection were considered but deemed nonpersuasive for the following reasons. Initially, it is noted that the above rejection was modified in response to applicant's amendment.

Applicant argues that Oshlack et al. fail to teach or suggest pharmacokinetic parameters with respect to dosage forms containing hydrocodone or a pharmaceutically acceptable salt thereof as recited in the present claims

This argument was considered but deemed nonpersuasive for the reasons recited in the above rejection e.g. Oshlack et al. teach controlled release formulation components suitable for a twice a day formulation of active agents (e.g. including hydrocodone), and means of altering these components (if necessary), to arrive at a composition that possesses (e.g. inherently) the presently claimed pharmacokinetic parameters.

Applicant further argues that "Oshlack et al. fail ... to teach ... or suggest" a dosage form hydrocodone or a pharmaceutically acceptable salt thereof suitable for twice a day administration comprising C12/Cmax ratio of 0.55 to 0.85.

This argument was considered but deemed nonpersuasive since the Oshlack reference clearly suggests hydrocodone or a pharmaceutically acceptable salt thereof suitable for twice a day administration (e.g see patent claims especially claims 1, 3, 6, 10-13 directed to twice a day hydrocodone controlled release dosage forms) with a teaching as to the use of a controlled release formulation, containing ingredients within the scope of applicants claims, which can be manipulated, if necessary, to achieve a twice a day formulation; and thus arrive at compositions which would necessarily possess (e.g. inherently) the presently claimed pharmacokinetic parameters (e.g C12/Cmax ratio of 0.55 to 0.85).

Applicant argues one of ordinary skill in the art would look toward MS CONTIN since "MS CONTIN is the only formulation described in the Examples of Oshlack et al. which could be related to the formulations of the present invention" since it is "a known 12 hour opioid formulation suitable for twice a day administration". Using Examples 19-20, Table 26 and Fig. 8 applicant calculates a C12/Cmax ratio of 0.16 which is outside that presently claimed.

Applicant's argument is nonpersuasive for several reasons.

First, Oshlack et al. use MS CONTIN for purposes of comparing the Oshlack's improved compositions to that of the prior art. Accordingly, MS CONTIN is NOT representative of the Oshlack reference compositions and one of ordinary skill in the art would not look to MS CONTIN if one wished to practice THE OSHLACK disclosed or CLAIMED INVENTION. In fact one of ordinary skill in the art would look to the Oshlack disclosure as described in the above rejection. The Oshlack disclosure (including the examples) teaches obtaining a "desired therapeutic effect for **about 12 hours** (emphasis provided) to about 24 hours" (e.g. see col. 5, especially lines 5-15) by utilizing "controlled release coatings" which comprise "Hydrophobic acrylic polymers" which preferably include "Eudragit RL/RS"; with the desired release profile being easily obtained by "changing the relative amounts of different acrylic resin lacquers included in the coating" (e.g. see col. 9-10). Additionally, optimal dissolution profiling can be obtained by "increasing or decreasing coating thickness. ..", "altering the manner in which the plasticizer is added... " (e.g. see col. 13). Accordingly, the reference teaches one of ordinary skill in the art how to make the Oshlack disclosed and claimed hydrocodone formulations suitable for twice-a-day

administration. Accordingly, one of ordinary skill would not turn to MS CONTIN for determining a twice a day formulation since it is a less desirable prior art formulation (e.g. MS CONTIN); and more importantly is clearly outside of the scope of the Oshlack patent claims. Interestingly, applicant's argument fails to indicate what compositional feature (e.g. coating components and proportional amounts, if present) would motivate one of ordinary skill in the art to consider MS CONTIN in the context of the OSHLACK et al. disclosed and claimed invention. Additionally, it is further noted that applicant has failed to attempt to calculate any C12/Cmax (or other pharmocological parameters) for any of the Oshalck et al. exemplified embodiments. It would appear to the examiner that the examples would be more instructive to one of ordinary skill in the art as to how to make a twice daily oral hydrocodone formulation which are within the OSLACK reference teaching. In this regard applicant may consider Example 19 and 20 which were compared to MS CONTIN (e.g. Example 19A). It would appear to the Examiner that Examples 19 and 20, which the Examiner roughly calculated as having an @ C12/Cmax of .50 (2/4) and .61 (3.3/5.4) using the same Table and Figure used by applicant, would provide more guidance to one of ordinary skill in art as to formulating OSLACK reference compositions (e.g. hydrocodone) which render obvious oral formulations "suitable for twice a day administration" (e.g. Example 19) and/or anticipate (e.g. Example 20), respectively.

Applicant finally argues that Oshlack et al. fails to teach, hint or suggest the various pharmacological parameters recited in the presently claimed invention.

This argument is nonpersuasive for reasons already provided and for the following.

Applicant's argument is not commensurate to the presently claimed invention which encompasses any oral dosage formulation of hydrocodone with controlled release material which is "suitable for twice a day administration" and which possesses a given pharmacological profile. Accordingly, applicant's argument is clearly non-responsive to the above 102/103 rejection's assertion that the Oshlack reference anticipates or renders obvious hydrocodone formulations which due to their compositional components necessarily meets the presently claimed pharmacological profiles. In other words, the reference anticipates or renders obvious solid oral hydrocodone controlled-release formulations (or their manufacture) that comprise analgesically effective amounts of hydrocodone (or salt thereof) and which contain "controlled release material" which meet applicant's claimed pharmacological profile(s). Applicant has not rebutted this fact, nor has applicant attempted to make a comparison (declaration or otherwise) between the patented Oshlack compositions (NOT MS CONTIN which is NOT an Oshlack composition) and those compositions within the scope of the presently claimed invention. In this regard, the Oshlack disclosure, Examples and claims taken as a whole to one of ordinary skill in the art clearly encompass "controlled release material " and active ingredients (e.g hydrocodone) "suitable for twice a day administration which are clearly within the scope of the presently claimed invention. It is noted that the Patent Office lacks the facilities to make comparisons between claimed and prior art compositions.

Accordingly, the above 102/103 rejection is hereby maintained.

New Objection (s) and/or Rejection (s)

4. Claims 16-18, 20, 27, 33 and 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims have been amended to contain the trademark/trade name LORTAB . Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name LORTAB is used to identify/describe and, accordingly, the identification/description is indefinite.

Conclusion

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

General information regarding further correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Celsa whose telephone number is (703) 305-7556.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang (art unit 1639), can be reached at (703)306-3217.

Any inquiry of a general nature, or relating to the status of this application, should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Bennett Celsa (art unit 1639)

September 10, 2003

BENNETT CELSA
PRIMARY EXAMINER